Product Data Sheet

Product Name: GSK2292767
Cat. No.: GC15679

Chemical Properties

Cas. No.	1254036-66-2		
Chemical Name	N-(5-(4-(5-(((2R,6S)-2,6-dimethylmorpholino)methyl)oxazol-2-yl)-1H-indazol-6-yl)-2-methoxypyridin-3-yl)methanesulfonamide		
SMILES	CS(=O)(NC1=CC(C2=CC3=C(C(C4=NC=C(CN5C[C@@H](C)O[C@@H](C)C5)O4)=C2)C=NN3)=CN=C1OC)=O		
Formula	$C_{24}H_{28}N_6O_5S$	M.Wt	512.58
Solubility	DMF: 16 mg/ml,DMF:PBS(pH7.2) (1:2): 0.3 mg/ml,DMSO: 14 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	GSK2292767		

Background

pKi: 10.1

GSK2292767 is a potent and selective PI3Kδ inhibitor.

Phosphoinositide 3-kinase δ (PI3Kδ), a lipid kinase belonging to the class 1 PI3K family with the closely homologous isoforms α and β, catalyzes the phosphorylation of phosphatidylinositol 4,5-bisphosphate, triggering various downstream biological events suvch as cell growth, proliferation, differentiation, and survival.

In vitro: GSK2292767 was found to be greater than 100-fold selective against a panel of in-house kinases and in the Millipore panel. Moreover, GSK2292767 could inhibit both IFNγ and IL-2 production in a concentration-dependent manner in a human lung parenchyma assay, with pIC50s of 8.7 and 8.5, respectively [1].

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In vivo: In a rat PK study, the in vivo clearance for GSK2292767 was significantly higher than that for its analog GSK2269557. The oral bioavailability was also low (F < 2%), which was consistent with the data observed for GSK2269557. In a rabbit cardiac ventricular wedge assay, no effect on QT interval, Tpe, or QRS and no significant risk of TdP arrhythmias was observed for GSK2292767 over the concentration range tested, thus indicating GSK2292767 could successfully mitigate the risk associated with GSK2269557. Moreover, GSK2292767 was found to protect against eosinophil recruitment with an ED50 of 35 μg/kg in the brown Norway rat acute OVA model, which was similar to GSK2269557 [1].

Clinical trial: The safety, tolerability and pharmacokinetics of single and repeat soses of GSK2292767 in healthy participants smokinf cigarettes is proposed, but this study is not yet open for participant recruitment [https://clinicaltrials.gov/ct2/show/NCT03045887].

Reference:
[1] Down K et al. Optimization of Novel Indazoles as Highly Potent and Selective Inhibitors of Phosphoinositide 3-Kinase δ for the Treatment of Respiratory Disease. J Med Chem. 2015 Sep 24;58(18):7381-99.

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